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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,594	06/22/2001	Vassilios Papadopoulos		6687

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/762,594	PAPADOPOULOS ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 02 January 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☐ The a)☐ affidavit, b)☐ exhibit, or c)☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: *10-16,41,48 and 49*.

   Claim(s) objected to: _____.

   Claim(s) rejected: *42-47 and 50-76*.

   Claim(s) withdrawn from consideration: _____.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Continuation of 2. NOTE: The recitation of "interacting with" in claims 42, 45, 53-56, 65-68 would raise a new issue under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "interacting with" in claims 42, 45, 53-56, and 65-68 is a relative term which renders the claims indefinite. The term "interacting with" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The term "interacting with" renders the claims broader, requiring additional consideration and/or search.

If the amendment of 02 January 2004 had been entered, the rejection of claims 42-47 and 53-76 under 35 U.S.C § 112, first paragraph (enablement and written description) would have been *withdrawn in part* in view of the claim amendments. The rejection of claims 50-52 under 35 U.S.C. § 112, first paragraph (total lack of enablement would have been withdrawn. Finally, the rejection of claims 45-47 and 65-76 under 35 U.S.C. § 112 second paragraph would have been withdrawn.

However, even if the amendment of 02 January 2004 had been entered, claims 42, 44-45, 47, 53-56, 61-68, and 73-76 would have remained rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid comprising a nucleic acid sequence that is at least 90% identical to the sequence of the nucleic acid sequence of claim 41 and encodes a polypeptide that impairs cholesterol delivery, does not reasonably provide enablement for a nucleic acid sequence that encodes a polypeptide that is capable of mediating cholesterol delivery or interacts with a peripheral-type benzodiazepine receptor (PBR). The specification is also not enabling for an isolated nucleic acid that encodes a polypeptide that is capable of interacting with a PBR or mediating cholesterol delivery and hybridizes to the complement of the nucleic acid of claim 41. Applicant asserts that a partial PAP7 fragment decreased the level of progesterone biosynthesis in Example 5, also inhibited pregnenolone formation in the inner mitochondrial membrane of MA-10 Leydig cells (Li et al. Molec Endocrinol 15:2211-2219, 2001; pg 2219). Applicant contends that inhibition of pregnenolone formation is due to a decrease accumulation of cholesterol at the inner mitochondrial membrane and reflects PAP7's ability to mediate cholesterol. Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, Li et al. states that overexpression of a partial PAP7 *inhibits* hormone-stimulated cholesterol transport (pg 2211, abstract; pg 2223, bottom of col 1; Fig 10). (It is noted that support for impairing cholesterol delivery/transport is found at the top of pg 4 of the specification.) Applicant also argues that the biological activity of PAP7 to directly bind PBR is fully enabled by the specification. Applicant indicates that PBR binding domains were identified (pg 16-17) and PBR binding domains of PAP7 interacted with PBR (Figure 3D o Li et al., PAP7 binds to PBR). Applicant's arguments have been fully considered but are not found to be persuasive. Although PAP7 (amino acids 216-445) may bind PBR, this binding does not indicate the biological activity or function of PAP7. Furthermore, as mentioned in the previous Office Action, Sher et al. (J Biol Chem 274(49):35016-35022, 1999) demonstrate that point mutations in a loop of FGF-7 do not alter receptor binding affinity, but cause reduced mitogenic potency and reduced ability to induce receptor-mediated phosphorylation events (pg 35020-35021).

If the amendment of 02 January 2004 had been entered, claims 42, 44-45, 47, 53-56, 61-68, and 73-76 would have remained rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant asserts that the specific biological activities of interacting with PBR and mediating cholesterol delivery are described in the specification or in the later published results of Li et al. and are to be correlated with the claimed variant. Applicant contends that the instant application is analogous to Example 14 of the Written Description Guidelines since the specific activity of PBR binding and cholesterol transport mediation is sufficiently disclosed in the application and this activity is required in the variant nucleic acid claims. Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, only an isolated nucleic acid comprising a nucleic acid sequence that is at least 90% identical to the sequence of claim 41 and encodes a polypeptide that impairs cholesterol delivery, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. As discussed previously, the fact pattern in the instant application is not analogous to Example 14 in the Revised Interim Written Description Guidelines. In Example 14 of the Guidelines, the protein and variants have a specific activity disclosed in the specification. However, regarding the PAP7 polynucleotides and polypeptides, the specification does not teach any significance or functional characteristics of all possible PAP7 polynucleotide sequences that are 90% identical to the sequence of the nucleic acid sequence of SEQ ID NO: 2 or to the nucleotide sequence that encodes the polypeptide set forth in SEQ ID NO: 7.